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| EXAMINER | |
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| LEITH, PATRICIA A | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/774,092 | BROVELLI ET AL. | |
| | Examiner | Art Unit | |
| | Patricia Leith | 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3,6,7 and 23-26* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 6, 7 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/04/2009 has been entered.

Claims 3, 6-7 and 23-26 are pending in this application.

Newly submitted claim 26 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 26 is patentably distinct from the originally-examined claims:

The Invention of Group IV (i.e., claim 26) and Claims 3, 6-7 and 23-25 (Group I) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are independent since they are not disclosed as capable of use together, they have different modes of operation, they have

different functions, and/or they have different effects. One would not have to practice the various methods at the same time to practice just one method alone. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 26 is hereby withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 3, 6-7 and 23-25 were examined on their merits.

***Claim Objections***

Claims 3 and 23 are objected to because of the following informalities: Claims 3 and 23 were originally directed toward methods for determining optimal harvest window of Echinacea plants; however, have been subsequently amended through prosecution to include a step of preparing an extract. Hence, the method is no longer a method for determining optimal harvest window, but is also directed toward preparing an extract and thus, the preamble of the claim is

improper. However, it is also noted that the as step of both of these claims is making a standardized extract which has been rejected under 35 USC 112 First paragraph Written Description as set forth *infra.*

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6-7 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended claims 3 and 24 (from which all of the other claims being examined depend directly or indirectly therefrom, respectively) to recite 'at least about 3.40%.' The term "at least about" in claims 3 and 24 is a relative term which renders the claim indefinite. The term "at least about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Correction is necessary.

Claims 3, 6-7 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: Each of claims 3 and 23 recite 'a method for determining optimal harvest window,' however, there is no step in either of claims 3 or 23 which teaches how to obtain an optimal harvest 'window.' Rather, the steps of these claims teach how to select a *maturation stage* of Echinacea. The term 'window' is much broader in scope than 'maturation stage' and it is not understood if Applicants intend for the term window to mean 'maturation stage.' It is suggested that claims 3 and 23 be amended to recite methods for selecting a maturation stage of Echinacea rather than an 'optimal harvest window' in order to overcome this rejection.

Claims 3, 6-7 and 23-25 recite 'and the highest level of immune-stimulatory product and preparing a standardized extract of the Echinacea plant at the selected maturation stage.' Here, it is seen that the maturation stage is selected by choosing two characteristics 1) that the Echinacea preparation is selected having a standardized concentration of at least about 3.40% and 2) the highest level of immune-stimulatory product. This is confusing. Several

maturation stages may have concentrations of at least about 3.40%, so if one chooses one of those maturation stages, is the maturation stage then selected from those maturation stages that have concentrations of at least about 3.40% or selected from another maturation stage? Hence, while the claims state selecting 'a' maturation stage or 'a' vegetative maturation stage, it appears that two maturation stages could potentially be selected.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 6-7 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the invention had possession, as of the filing date of the application, of the specific subject matter later claimed by him or her. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention.' Lockwood v. American Airlines, Inc., 107 F. 3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F. 2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F. 3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient" MPEP § 2163.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus MPEP § 2163. Although the MPEP does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. *In Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. .

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F. 2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outline [goals] appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed had possession of the entire scope of the claimed invention.

Specifically, claims 3 and 24 have been amended to read '(i) a standardized concentration of at least about 3.40 of either chlorogenic acid or chicoric acid…'. The disclosure, as filed, does not support this new limitation. First, the only disclosure of '3.40% in the original disclosure as filed is in Table 1 (p. 6, [0023]). This value is an observed value assessed from analyzing various maturation stages of Echinacea for chicoric acid content. Chlorogenic acid is not mentioned here. Additionally, the only mention of 'at least about' in the disclosure as filed, was original claim 21 which stated 'A preparation of Echinacea purpurea comprising: a standardized level of chicoric acid of at least about 3.49%.' Hence, the number here is 3.49 and not 3.40 and more importantly, claim 21 of the original claims is directed toward a standardized preparation, and not a method for measuring to determine optimal harvest time. With regard to Applicants' method for *determining their optimal harvest time*, it is not taken that Applicants contemplated an amount 'at least about' 3.40% which reaches well-beyond what Applicants have actually demonstrated in the Instant specification with regard to chicoric acid concentrations measured in each respective maturation stage (i.e., the highest concentration measured was 3.62%).

Secondly, there is nowhere in the Specification as filed that Applicants chose their maturation stage based upon any particular amount of chicoric acid or chlorogenic acid; rather, Applicants chose their maturation stage based upon the presence of chicoric acid and based upon the highest amount of immune-stimulatory product obtained via cell assay. Hence, the inclusion of a step wherein a maturation stage is selected with any particular amount of chicoric acid goes beyond what was originally disclosed as can be determined from the original disclosure *as a whole*.

Thirdly, claim 3 was amended on 9/19/2007 to require that a standardized extract is prepared from the selected maturation stage. As now claimed part (ii) of claims 3 and 23 recite 'and preparing a standardized extract of the Echinacea plant at the selected maturation stage.' However, the only extracts prepared in the specification were *prior to selection of the maturation stage*. The Examiner has considered the entire disclosure including the original claims. There is no disclosure, of which the Examiner can find in the original disclosure as filed whereby Applicants have prepared a standardized extract after determining their 'optimal' maturation stage.' Hence, absent convincing evidence and/or argument to the contrary, it is determined that Applicants were not in possession of this step at the time the invention was filed.

Because claims 6-7 and 24-25 depend directly or directly upon either of claims 3 or 23 respectively and because these claims do not remedy the

deficiencies of either of claims 3 or 23 respectively under this statute for lacking written description, these claims also comprise new matter and are properly rejected under this statute.

In order to overcome this rejection, Applicants are required to either delete the new matter in claims 3 and 23 or provide convincing evidence and/or arguments to establish that the limitation in question is present either explicitly or implicitly within the disclosure as filed.

Claims 3, 6-7 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining a maturation stage to harvest Echinacea plants, does not reasonably provide enablement for determining an *optimal harvest window* of Echinacea plants. Further, while the specification is enabled for a method for determining a maturation stage to harvest Echinacea plants, the specification is not enabled for 'selecting a maturation stage with a standardized concentration of at least about 3.40% of chlorogenic acid or chicoric acid and the highest level of immune-stimulatory product and preparing a standardized extract of the Echinacea plant at the selected maturation stage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The phrase 'optimal harvest window' is speculative. While Applicants have determined that *their* optimal harvest maturation stage is achieved through the steps set-forth in the claims; Applicants' have not provided evidence that their method will determine an 'optimal' harvest window or maturation stage for a

representative number of harvest times (or maturation stages). Echinacea is harvested for other purposes besides Applicants' purpose, and the skilled artisan working in the field of harvesting Echinacea may not consider Applicants' idea of 'optimal' their idea of 'optimal.' Considering that different artisans will have a different idea of what 'optimal' means to them as individuals, Applicants are not enabled for determining 'optimal' harvest window of Echinacea plants, or even for determining an 'optimal' maturation stage of Echinacea. For example, someone harvesting Echinacea for the florist industry would not consider Applicants' method an 'optimal' harvest 'window' because; in light of the specification (and claim 23 which specifically recites vegetative stage); these growers would not want to harvest their Echinacea in the vegetative stage to sell as cut-flowers.

***Rejections Removed***

The previous rejection instituted under 35 USC 112 First paragraph over claims 3, 6, 7 and 23-25 is hereby removed due to Applicants' amendment to the claims which removes the language 'that is used to prepare an extract of the Echinacea plant.' Applicants' additional arguments regarding this rejection are rendered moot due to the removal of the limitation which caused this rejection to be instituted.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 6-7 and 24 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Gahler et al. (US 6,511,683) in view of Letchamo et al. FACTORS AFFECTING ECHINACEA QUALITY; ASHS Press, Alexandria, VA (2002), Seidler – Lozykowska et al. (2003), Dou et al. (2001 – Abstract) and Rininger et al. (2000) .

Gahler et al. . (US 6,511,683) recognized the advantage of standardizing extracts of Echinacea for several desired endogenous compounds such as chicoric acid, alkylamides and polysaccharides (see entire patent and Abstract):

> [I]t is desirable to formulate Echinacea compositions to contain standardized amounts of biologically active components derived from Echinacea plants. Such standardized, Echinacea compositions provide the consumer with a consistent, effective dose of one or more, biologically active, Echinacea components. In particular, there is a strong commercial market for Echinacea extracts containing a high concentration of one or more, biologically active, Echinacea components believed to promote good health. Such highly enriched extracts can be used directly as dietary supplements, or can be blended with other Echinacea extracts to prepare dietary supplements containing standardized amounts of biologically active, Echinacea components. (col. 1, lines 23-37)

Gahler et al. clearly established the desirability of standardizing Echinacea for several markers in order to produce extracts with added medicinal benefit (see column 1):

> Scientific studies indicate that Echinacea-derived polysaccharides, alkylamides and chicoric acid (a caffeic acid derivative also known as chicoric

> acid, 2,3-o-di-caffeoyl-tartaric acid) each possess health-promoting properties. For example, alkylamides from Echinacea have been shown to stimulate phagocytosis in mice granulocytes at concentrations of about 0.1 parts per million (ppm). Bauer, R. et al., Arzneim.-Forsch./Drug Research, 38: 276-281 (1988). Similarly, chicoric acid has been shown to increase phagocytosis in granulocytes, and may stimulate the immune system at concentrations as low as 0.01 ppm. See e.g., A. Awang et al., supra. Echinacea polysaccharides have been shown to inhibit hyaluronidase, increase phagocytosis, induce the release of interferon-6, and enhance resistance to C. albicans infection in mice. See, e.g., A. Awang et al., supra; Wagner, H, et al. Arzneim.-Forsch./Drug Research, 35: 1069-1075 (1985).
>
> (7) Numerous factors must be considered and optimized in order to produce Echinacea extracts having a high concentration of polysaccharides, alkylamides and/or chicoric acid. For example, the amounts of polysaccharides, alkylamides and chicoric acid in Echinacea plants are influenced by the species of the plant, the age of the plant and the plant growth conditions. Additionally, the solvents and process parameters, such as temperature and length of extraction period, utilized to extract polysaccharides, alkylamides and chicoric acid from Echinacea plants can greatly affect the yield of these components.
>
> (8) Thus, there is a need for methods for efficiently extracting polysaccharides, alkylamides and chicoric acid from Echinacea plants, and for Echinacea extracts containing a high concentration of polysaccharides, alkylamides and/or chicoric acid. Further, there is a need for standardized Echinacea compositions containing a predetermined, desired amount of Echinacea extracts, including polysaccharide, alkylamide and/or chicoric acid extracts.

Gahler et al. additionally recognize the importance of selecting an Echinacea plant at a particular growth stage with the desired amounts of each analyte marker compound (see col. 2, and columns 11-12 for example). Here, Gahler et al. provides detailed information of how to select Echinacea for optimum analyte concentration.

Gahler et al. clearly established that their extracts containing multiple marker compounds influenced immune system parameters such as IL-2 and

TNF-α (*inter alia*) (see, for example, Figures 1-7 and 'Brief Description of the Drawings').

Gahler et al. did not specifically teach where Echinacea plants were harvested at different maturation stages and added to a cell culture to analyze immune products or translation products induced by Echinacea, or wherein a stage of maturation was selected which had a standardized concentration of 'at least about 3.40% chicoric acid' and the highest level of immune-stimulatory product.

Letchamo et al. FACTORS AFFECTING ECHINACEA QUALITY; ASHS Press, Alexandria, VA (2002) teach that Echinacea is "…among the most frequently utilized medicinal herbs around the world" known for treating cold, cough and sore throats (p. 514). Letchamo et al. indicate that the pharmacological activity/chemical content of common markers (such as chicoric acid)of Echinacea extracts vary significantly upon choice of soil selection, disease, insect infestation, climate, country of origin and harvest time (see entire reference, especially p. 514, 515, Table 1, , Table 3, and Table 4). Letchamo et al. show that chicoric acid content as a percentage of dry matter varies with regard to the country of origin, with Russian cultivars producing the highest yields of chicoric acid (Table 1). Letchamo et al. clearly demonstrate the nexus between harvest time and chicoric acid content: Table 4 reports the effects of

flower developmental stages on chicoric acid content. Table 4 demonstrates that chicoric acid levels of E. purpurea at the early flower developmental stages produce the optimum amount of chicoric acid of 3.97% (see Table 4). The authors establish that they suggest that a 2.2% level of chicoric acid concentration for any standardized *E. purpurea* material (see p. 520 under Conclusions).

Echinacea was well known in the art for imparting immunological activity of macrophage cells according to Rininger et al. (2000). Specifically, Rininger et al. analyzed the production of TNF- α, IL-1α, IL-1βIL-6, IL-10 and nitric oxide from macrophage cells upon contact with several products of Echinacea including standardized extracts, whole plant material, juice and phenolic compounds (see entire reference, especially pages 4-10). Rininger et al. specifically stated that "Echinacea immunostimulatory activity varied significantly from lot-to-lot of raw material from the same supplier and may reflect growth conditions, time of harvest, milling and storage conditions" (p. 10).

Seidler – Lozykowska et al. (2003) analyzed the polyphenolic acid content of Echinacea purpurea during various growth stages of the plant (see Abstract and Material and Methods). Seidler – Lozykowska et al. determined that "the highest concentration [of polyphenolic acids] was in the leave blades…during flowering stem formation in one year plants".

Dou et al. (2001- Abstract) taught assaying the level of chicoric acid in *Echinacea purpurea* plant material in different stages of growth (see Abstract). Dou et al. indicated that "The content of chicoric acid and yield were the highest in the overground part of *E. purpurea* before and after the bloomy stage" (Abstract).

Echinacea was well known in the art for imparting immunological activity of macrophage cells according to Rininger et al. (2000). Specifically, Rininger et al. analyzed the production of TNF- α, IL-1α, IL-1βIL-6, IL-10 and nitric oxide from macrophage cells upon contact with several products of Echinacea including standardized extracts, whole plant material, juice and phenolic compounds (see entire reference, especially pages 4-10). Rininger et al. specifically stated that "Echinacea immunostimulatory activity varied significantly from lot-to-lot of raw material from the same supplier and may reflect growth conditions, time of harvest, milling and storage conditions" (p. 10).

The desirability of creating Echinacea extracts with increased immunopotentating activity, as well as increased levels of compounds such as chicoric acid was *well-documented in the art* (see cited references, especially Gahler et al.). It is deemed that the method claims of the Instant invention would have been well-within the purview of the ordinary artisan at the time the invention was made having the above-cited references before him or her. One of ordinary skill in the art would have had a reasonable expectation of success in choosing

an Echinacea plant with 'the highest' amount of immuno-stimulatory' activity and at least some amount of chicoric acid because both immuno-stimulatory activity as well as chicoric acid were desired at the time the invention was made.

One of ordinary skill in the art would have been motivated to harvest Echinacea at different growth stages to ascertain its immunopotentiality on macrophage cells in order to assess immuno-function of the plant at different stages. Analyzing Echinacea plants at different stages for particular immuno-potentiating compounds was known in the art according to Letchamo et al., Dou et al. and Seidler – Lozykowska et al. (2003), and Rininger et al. recognized that the variance of immunostimulatory activity was probably due to time of harvest *inter alia.* Thus, the ordinary artisan would have had a reasonable expectation that testing the Echinacea at varying growth stages for immunopotentating activity would have determined an optimum harvest time for the Echinacea.

It is clear from Rininger that what was investigated was immunostimulatory activity of Echinacea; via quantitatively assessing transcriptional products (cytokines) produced by RAW 264.7 cells in response to contact with Echinacea. Therefore, what was known in the art at the time the Invention was made was that Echinacea had immunostimulatory properties which were scientifically investigated. What was further known in the art was that Echinacea could be tested *in-vitro* for immunopotentating ability by measuring

transcriptional products such as TGF and IL produced by RAW 264.7 cells. Therefore, it was well known at the time the Invention was made that amount of these transcriptional products produced by RAW 264.7 cells were proportional to the plant's immuno-potentiating activity (see Rininger et al., Figures 1 and 2 for example). Rininger et al. further specifically stated that that "Echinacea immunostimulatory activity varied significantly from lot-to-lot of raw material from the same supplier and may reflect growth conditions, time of harvest, milling and storage conditions" (p. 10). Again, analyzing Echinacea plants at different stages for particular immuno-potentiating compounds and chicoric acid was well-known in the art . Therefore, the ordinary artisan would have been motivated to determine the optimal harvest window of Echinacea in order to obtain plant material which possessed maximum immunopotentating effects.

It is noted that the prior art does not specifically teach all of the claim limitations in one reference, hence, there is no 102 rejection. However, the invention as a whole is rendered obvious by the prior art references. Echinacea plants were well-known in the art at the time the invention was made and exhaustively studied for their medicinal effects. The claimed invention as a whole is obvious, and there is no individual step in any of the method claims which was not already known or made obvious by the prior art. That is, there is no novel step or idea in the method claims which makes it unobvious over the prior art references. According to the prior art references, as keenly pointed out in the previous Office actions, Echinacea plants were known to be studied at

different maturation stages for marker compounds to select for optimum levels of compounds. Echinacea plants were also known to contain immunopotentating activity, and the activities were known to be studied and already determined to depend, in part, upon the harvesting time of the Echinacea. Harvesting Echinacea plants in the vegetative stage was known, due to the level of chicoric acid in the flowers at this stage of plant maturation. Additionally, Applicants' method for determining the level of immunopotentating activity, as well as marker immuno stimulatory products were known in the art at the time the invention was made. While no one, individual reference taught all of these steps together; the ordinary artisan would have been motivated to perform the claimed method in order to optimize medicinal efficacy of an Echinacea extract and standardization would have been routine in manufacturing extracts with essentially uniform chemical constituents and hence, medicinal effectiveness: *"[a] person of ordinary skill is also a person of ordinary creativity, not an automaton* *KSR* 127S. Ct. at 1742 (emphasis added).

. Letchamo et al. makes plainly evident that that selection of marker compounds such as chicoric acid present at the claimed amount ('at least about 3.40%) were already known in the art through their routine experimentation to test chicoric acid levels in different maturation stages of Echinacea plant growth. Letchamo et al. further offer that chicoric acid should be standardized to at least 2.2%. Hence, while Applicants found that in their investigation, a particular plant of Echinacea purpurea at the vegetative stage contained 3.49% of chicoric acid

and the maximum amount of immunopotentating activity; this data is not found to be significant and is not considered to be reproducible considering that Applicants did not disclose specific growing conditions of Echinacea; in other words, the chicoric acid content and immunopotentating activity will inevitably be different from plant to plant. It is expected that different maturation stages of Echinacea will produce optimum amounts of chicoric acid and optimum results when assayed for immunopotentating activity. As reiterated throughout this prosecution, it is evident that in Applicants' study, the level of chicoric acid was relatively consistent throughout maturation stages. Now, as claimed, the method requires that a maturation stage is selected which comprises at least 3.40% of chicoric acid and a highest level of immune-stimulatory product. The claims are deemed obvious and well-within the skill level of the ordinary artisan at the time the invention was made. Applicants' claims, even though reciting 'consisting essentially of' are broad enough to read on wherein an ordinary practitioner harvests Echinacea at least two maturation stages and selects, for example, two maturation stages, each having a chicoric content above 3.40% as required by the claim; for example, one could have 4.0% and the other could have 5.0%. It would have been clearly obvious to one of ordinary skill in the art to chose the maturation stage between these two maturation stages which has the highest amount of chicoric acid and the highest potentiating activity.

It is deemed that the method as claimed is an obvious variation of known methods to produce extracts of Echinacea having maximum amounts of chicoric

acid and immuno-potentiating effects. To arrive at the claimed invention would have been well-within the purview of the ordinary artisan having the above- cited references before him or her, and could have been achieved through routine experimentation.

***Response to Argument***

Applicants cite the Graham factual inquiries and assert that these tenants must be adhered to upon instituting a rejection under 35 USC 103(a) (p. 8, Remarks). The Examiner agrees, and asserts that the Graham factual Inquires have been adhered to upon placing the rejections set forth *supra*.

Applicants argue that the prior art 'teaches away' from the claimed invention because Applicants allege that the prior art teaches that Echinacea extracts standardized using chicoric acid or chlorogenic acid as marker compounds do not exhibit immunopotentating activity (pp. 9-10, Remarks). Applicants specifically point to Gahler and argue that Gahler teach that "…an Echinacea extract standardized with primarily chicoric acid as the marker compound or polysaccharides as the marker compound do not display significant immunostimulatory activity…" Applicants cite the teachings of Gahler which indicate that chicoric acid and polysaccharides as the marker compound did not display significant immunostimulatory activity (pp. 10-11, Remarks). However,

first it is noted that the claims do not require a 'significant' immunostimulatory effect; rather, the claim merely recites choosing a maturation stage with the highest level of immune stimulation out of the different samples of maturation stages tested. Additionally, the chicoric acid tested by Gahler was essentially purified, and it has already been established on the record that chicoric acid is not specifically the compound which produces immuno-potentiating activity.

Applicants are directed toward their claims which are directed toward a method for determining an optimal harvest window for Echinacea. The steps of the method (e.g., claim 1) include harvesting Echinacea at various maturation stages, determining chicoric acid content, determining levels of immuno-stimulatory product through a cell assay and choosing a maturation stage with a level of chicoric acid which is at least about 3.40% and the maturation stage having the highest level of immune-stimulatory product and further preparing a standardized extract from the selected maturation stage. Again, testing for chicoric acid levels at different maturation stages was known in the art and immunopotentating activity had already been linked to harvest time. One of ordinary skill in the art would readily recognize from the prior art that Echinacea plants contain immuno potentiating activity; whether it be manifested from polysaccharides or alkylamides or some other endogenous phytochemical in Echinacea (e.g., see Fig. 5 of Gahler and Col. 4, lines 48-58) and that these phytochemicals would be present in the Echinacea plant. The claims are merely

testing for optimal harvest time and preparing a standardized extract; the claims are not directed toward what the extract is standardized for.

The Echinacea plant chosen in Applicants' method claims will have immuno-potentiating activity, because the *plant contains all of the immuno-potentiating compounds*. The ordinary artisan, having the above-cited references before him or her, and thus possessing the knowledge that Echinacea comprises highly sought-after chicoric acid as well as immuno-potentiating activity would have been motivated to determine the optimal harvest 'window' (or maturation stage) of their Echinacea crop based upon cell assays on various harvest times to determine immunopotentating activity and chicoric acid content to maximize immunopotentating activity and chicoric acid content. One of ordinary skill wishing to do this, might be interested in selling the plant whole; e.g., as in a dry powder form. Again, the claim is directed toward selection of a particular maturation stage and preparation of a standardized extract. Thus, the claim is broad enough to read on preparing a powder of a plant chosen at the particular maturation stage or preparing an extract standardized for any phytochemical or immunopotentating activity. Hence, the ordinary artisan would have had a reasonable expectation of success in using the claimed invention to ascertain their own optimal maturation stage seeing that 1) Echinacea was known to be tested at various levels for chicoric acid content and 2) that Echinacea was known to have immuno potentiating activity. Thus, Applicants' arguments pertaining to Gahler which teach that chicoric acid does not produce

significant immunostimulatory effects is not found particularly pertinent and is not convincing to overcome the outstanding rejections.

Similarly, on p. 11, Applicants argue "…when Gahler is viewed in connection with Rininger…it is clear that one of ordinary skill in the art would have no reasonable expectation of success in achieving a method of obtaining an *Echinacea extract* having the highest level of immune-stimulatory compounds and a standardized concentration of chlorogenic or chicoric acid." (emphasis added) However, the claims are not directed toward obtaining an extract with the highest levels of immune-stimulating compounds or a standardized concentration of chlorogenic or chicoric acid. Hence, Applicants appear to be arguing limitations which are not claimed. Whether or not the extracts of the prior art were standardized or not bears little or no relation to whether or not the claims are obvious over the cited references because the claims are not directed toward extracts which are standardized for any particular compounds or levels of chicoric acid.

Again, in response to Applicants' allegations toward Rininger, Rininger chose a random standardized extract of Echinacea; standardized for chicoric acid and found that it did not have immunopotentating activity (Remarks pp. 11-12). Again, this does not negate the fact that it was known that Echinacea contained chicoric acid and immunopotentating activity. This teaching of Rininger does not overcome this rejection because, again, it is not deemed

particularly pertinent to the rejection which is based upon claims directed toward a method for determining optimal harvest window of Echinacea and preparing a standardized extract of Echinacea from the selected maturation stage. Further, an extract standardized for chicoric acid can have immunopotentating activity; the only reason the extract of Gahler did not have immune-potentiating activity is because Gahler essentially purified their extract for chicoric acid. Someone choosing a harvest time based upon the highest level of chicoric acid would have found it obvious to also assay their harvested samples for immuno-potentiating activity.

Applicants' arguments presented on pp. 12-13 essentially their previous arguments, that since the prior art does not teach standardized extracts of chicoric acid produce an immunological effect, that the prior art fails to render the claimed invention *prima facie* obvious. However, to reiterate from above, the claims are not directed toward a method for making any particular extract of Echinacea; rather, they are directed toward selection of an optimal harvest window to harvest Echinacea and preparation of a standardized extract of Echinacea (which can mean standardized for anything at any level). The techniques found in the claims; e.g., assaying for chicoric acid levels and cell assays to determine amounts of immuno-products produced from cell assays with regard to Echinacea were well-known in the art. Optimizing harvest times based upon chicoric acid content was well-known in the art and Rininger specifically suggested that immunopotentating activity was affected by harvest

time. Hence, having the knowledge of the prior art, one of ordinary skill in the art, wishing to obtain an optimal harvest time of Echinacea would have been motivated to perform the claimed method steps. And to reiterate from above, although each method step was not explicitly taught in one prior art reference; considering the knowledge pertaining to Echinacea as set forth keenly *supra*, it is determined that the claimed method steps could have been achieved through routine optimization of prior art methods for determining optimal harvest time of Echinacea.

"Common sense teaches … that familiar items may have obvious uses beyond their primary purposes, and in many cases a person or ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *KSR*, 127 S.Ct. at 1742. *See also, Muniauction, Inc. v. Thomson Corp.*, ___ F.3d ___, 2008 WL 2717689, at *6-*10 (Fed. Cir. July 14, 2008); *Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1160-63 (Fed. Cir. 2007).

The Supreme court has acknowledged that:

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. **If a person of ordinary skill can implement a predictable varition..103 likely bars its patentability**…if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions…

…**the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results** (see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007) emphasis added.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

## ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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